

Applicants: Kenneth A. Jones, et al
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1. Support for claim 161-162 may be found inter alia in the specification, as originally-filed, on page 30, lines 30-35. Support for claims 163-165 may be found inter alia in the specification, as originally-filed, on page 31, lines 1-12.

Support for claims 166-168 may be found inter alia in the specification, as originally-filed, on page 31, lines 14-24. Support for claims 169-171 may be found inter alia in the specification, as originally-filed, on page 31, line 26 through page 32, line 2. Support for claims 172-174 may be found inter alia in the specification, as originally-filed, on page 32, lines 4-17. Support for claim 175 may be found inter alia in the specification, as originally-filed, on page 32, lines 19-27; page 98, line 15; and Figure 2. Support for claims 176-178 may be found inter alia in the specification, as originally-filed, on page 29, lines 1-5; page 36, lines 20-34; page 78, line 6 through page 80, line 27.

Support for claims 179-181 may be found inter alia in the specification, as originally-filed, on page 32, line 29 through page 33, line 5. Support for claims 182-183 may be found inter alia in the specification, as originally-filed, on page 33, lines 7-12.

Accordingly, applicants respectively request that this Amendment be entered.

A. Election/Restrictions

On page 2 of the February 8, 2002 Office Action, the Examiner stated that applicants election with traverse of Group I is not persuasive because allegedly the nucleic acids of Groups I-VI are structurally and functionally distinct and would require a separate search of the art. The Examiner alleged that each

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distinct group requires a separate field of search, and a search of one Group would not reveal art on the other Groups, thus imposing a burden on the Examiner.

The Examiner then concluded that the requirement is still deemed proper and is therefore made final.

B. Rejection under 35 U.S.C. §112, first paragraph

On page 4 of the February 8, 2002 Office Action the Examiner rejected claim 6 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner alleged that due to the limitation of "genomic DNA" recited in the claim, a determination of what the claim as a whole covers indicates that elements which are not particularly described, for example promoters, enhancers, untranslated regions and introns, are encompassed by this claim. The Examiner then alleged that there is no actual reduction to practice of the claimed invention, or complete description of the structure. The Examiner concluded that one skilled in the art would not recognize from the disclosure that the Applicant was in possession of the claimed invention.

In response, in order to advance the prosecution of the subject application, but without conceding the Examiner's position, applicants have canceled claim 6, and replaced it with new claim 159. New claim 159 recites "...wherein the DNA is genomic DNA and consists essentially of nucleotides encoding the chimeric G protein". Applicants maintain that new claim 159 no longer covers those elements associated with genomic DNA, i.e. promoters,

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enhancers, untranslated regions and introns, and that new claim 159 only encompasses the coding region of the chimeric G protein.

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this portion of the rejection.

On page 4 of the February 8, 2002 Office Action the Examiner rejected claims 1-22 under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding a chimeric G protein wherein the G protein has the amino acid sequence set forth in SEQ ID NO: 1, allegedly does not provide enablement for isolated nucleic acids encoding chimeric G proteins which vary at least five, but less than twenty-one amino acids.

The Examiner alleged that claim 1 is overly broad in the recitation of "at least five, but not more than twenty one contiguous amino acids" since insufficient guidance is provided as to which of the nucleic acid species encoding the myriad of polypeptide species encompassed by the claim will retain the characteristics of a Gαq subunit, since no functional limitation is recited in the claim.

The Examiner cited examples of proteins known in the art that do not retain their original function when mutated at only one amino acid.

The Examiner then alleged that the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The Examiner then concluded that given the breadth of claims 1-22 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance

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provided in the instant specification and the prior art of record, it would require undue experimentation for one of an ordinary skill in the art to make and use the claimed invention.

In order to advance the prosecution of the subject application, but without conceding the Examiner's position, applicants have canceled claims 1-22, and added new claims 156-183. Applicants maintain that new claims 156-183 satisfy the enablement requirement. Applicants direct the Examiner's attention to new claim 156, which recites,

"An isolated nucleic acid encoding a chimeric G protein, wherein the chimeric G protein comprises an invertebrate G α q G protein from which at least five, but not more than twenty-one, contiguous amino acids beginning with the C-terminal amino acid have been deleted and replaced by a number of contiguous amino acids present in a vertebrate G protein beginning with the C-terminal amino acid of such vertebrate G protein, wherein such number equals the number of amino acids deleted; provided that the chimeric G protein, upon activation, produces a G α q second messenger response."

Applicants maintain that new claim 156 provides a functional limitation for the subject chimeric G protein. Applicants further maintain that given the content of the disclosure of the subject application, the examples provided by the disclosure and the prior art, the predictability of the art is high and therefore one skilled in the art would have a reasonable expectation of success to practice the claimed invention without undue experimentation.

Applicants point out that G α proteins possess two functionally distinct domains: 1) a G protein-coupled receptor (GPCR) recognition site and 2) a GTP-binding domain. The GPCR recognition site is known in the art to be located at the extreme C-terminal region of the G α protein. See the specification as

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originally filed on page 5, lines 11-30. The remainder of the G α protein, excluding the extreme C-terminal region, is referred to as the "backbone" of the G α protein. The G α protein backbone contains the GTP-binding domain, or effector coupling site, which specifies effector signaling. It has been demonstrated by Vankatakrisman and Exton et al (1996), a copy of which is attached hereto as **Exhibit A**, that for the hamster G α_q protein, the region between amino acid residues 217-276 (contained in the G α_q protein backbone) was required for phospholipase C activation (a typical G α_q second messenger response).

Applicants note that it is well known in the art that a G α_q protein functions by eliciting a second messenger response, i.e. the activation of the phospholipase C (PLC) signaling pathway. Activation of PLC can be measured by the release of inositol phosphate or by calcium mobilization. Applicants maintain that these and other second messenger responses are measured routinely in the art of pharmacology. Applicants maintain that contrary to the examples of deleterious protein mutations pointed out by the Examiner, the state of the art provides evidence that C-terminal mutations of the G α_q protein allow the G α_q protein to retain its function.

Applicants further maintain that the state of the art and the content of the disclosure of the subject application provide evidence that the predictability of the art is high. Applicant points out that the subject application provides examples of C-terminal deletions and substitutions comprising 5, 9 or 21 amino acids. See SEQ ID Nos: 1 through 5, and SEQ ID NO: 41. Applicant points out that the state of the prior art provides many examples of vertebrate chimeric G proteins, for example C-terminal deletions and substitutions comprising 5, 9, 10, 11, 13, 18 amino acids. See for example, Conklin et al (1993), attached hereto as

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Exhibit B. Based on the many examples of G α protein chimeras containing a vertebrate backbone, the predictability of the art is high. Applicants maintain that the expectation of success with chimeric G proteins having an invertebrate G α q backbone is even higher given the degree of amino acid homology between G α q proteins across several invertebrate species. See Figures 5A-5C of the instant application.

Accordingly, applicants maintain that new claims 156-183 satisfy the enablement requirement and undue experimentation is not required for the skilled person to make and use the subject invention. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the rejection.

On page 6 of the February 8, 2002 Office Action the Examiner rejected claims 1-22 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner alleged that this is a genus claim. The Examiner alleged that according to the specification, the term variant means a protein having one or more amino acid substitutions, deletions, insertions and/or additions made to SEQ ID NO: 1. The Examiner then alleged that the specification and claim do not indicate what distinguishing attributes are shared by the members of the genus. The Examiner also alleges that the specification states that these types of changes are routinely done in the art and that the specification and claim do not provide any guidance as to what changes should be made.

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In order to advance the prosecution of the subject application, but without conceding the Examiner's position, applicants have canceled claims 1-22, and added new claims 156-183. Applicants point out that claims 156-183 do not recite the term "variant". Applicants maintain that new claim 156 limits the number of chimeras in the claimed invention, whereas the number of C-terminal amino acids deleted equals the number of amino acids replaced at the C-terminus. Applicants point out that the specification provides several specific examples of the claimed chimeric G proteins, namely SEQ ID Nos. 1 through 5 and SEQ ID NO: 41. Furthermore, as discussed herein above with regard to enablement, the subject disclosure and the prior art provide further examples of chimeric Gαq proteins containing a vertebrate backbone.

In light of the remarks made herein above, applicant respectfully requests that this rejection be withdrawn.

C. Rejections under 35 U.S.C. §112, second paragraph

On page 8 of the May 8, 2002 Office Action, the Examiner rejected claims 1-22 for allegedly being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner alleged that claim recites the term "varies therefrom" which is a conditional term and renders the claim indefinite. The Examiner further alleged that there is insufficient guidance as to what specific sequences the term "varies therefrom" refers to. The Examiner stated that claims 2-22 are rejected insofar as they depend on the recitation of the term "varies therefrom".

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The Examiner then alleged that claim 22 recites the term "substantially" which is a relative term and renders the claim indefinite. The Examiner stated that this rejection could be obviated by supplying specific parameters supported by the specification which applicants consider to be "substantially".

In order to advance the prosecution of the subject application, but without conceding the Examiner's position, applicants have canceled claims 1-22, and added new claims 156-183. Applicants maintain that new claims 156-183 do not contain the terms "varies therefrom" or "substantially".

Accordingly, applicants respectfully request that this rejection be withdrawn.

On page 8 of the May 8, 2002 Office Action, the Examiner rejected claim 22 under 35 U.S.C. 102(b) as allegedly being anticipated by Maurice et al (1993). The Examiner alleged that Maurice et al teaches the cloning and expression of a turkey Gαq which is substantially the same as the nucleic acid sequence set forth in SEQ ID NO: 1. The Examiner alleged that claim 1 is anticipated.

In order to advance the prosecution of the subject application, but without conceding the Examiner's position, applicants have canceled claims 1-22, and added new claims 156-183. Applicant maintains that new claim 177 is not anticipated by Maurice et al. because new claim 177 does not recite the term "substantially". Applicants maintain that new claim 156 is not anticipated by Maurice et al. because Maurice et al. do not teach a chimeric G protein with an invertebrate Gαq backbone.

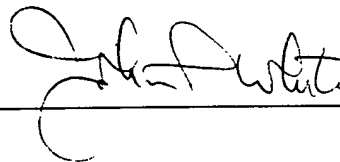
Accordingly, applicants respectfully request that the rejection under 35 U.S.C. 102(b) be withdrawn.

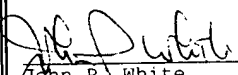
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If a telephone interview would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone the number provided below.

No fee, other than the enclosed fee of \$496.00 (\$36.00 for filing the Amendment and \$460.00 for filing the three-month extension of time), is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully Submitted,



I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.	
	8/8/02
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